UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

PDL BIOPHARMA, INC. and EKR THERAPEUTICS, INC.,	:	Honorable Katharine S. Hayden, U.S.D.J
	:	Civil Action No. 07 CV 1788 (KSH)(PS)
Plaintiffs,	:	
v.	:	
	:	**FILED UNDER SEAL**
SUN PHARMACEUTICAL INDUSTRIES LTD.	:	
	:	**Oral Argument Requested**
Defendant.	:	

REPLY BRIEF IN SUPPORT OF SUN'S MOTION FOR SUMMARY JUDGMENT OF NONINFRINGEMENT AND IN OPPOSITION TO PLAINTIFFS' CROSS-MOTION FOR SUMMARY JUDGMENT OF INFRINGEMENT

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INTRODUCTION

PDL's brief ignores a case-ending fact: Each claim of the '405 patent expressly requires the accused product to be *both* concentrated *and* isotonic, which permits direct injection with a low-volume syringe. Sun's accused product, however, cannot be directly injected because it is never both concentrated and isotonic at the same time. When concentrated, Sun's product is not isotonic and, thus, cannot be directly injected. When diluted for high-volume intravenous administration, Sun's product is not concentrated.

PDL does not and cannot avoid these facts. PDL never asserts that any single form of Sun's product meets both disputed limitations. When arguing that Sun's product is concentrated with "at least 1 mg/ml nicardipine hydrochloride," PDL focuses solely on the *concentrated* form of Sun's product. When arguing that Sun's product is "isotonic," PDL focuses solely on the *diluted* form. Thus, it remains undisputed that neither form of Sun's product literally infringes.

Instead of facing these irrefutable facts squarely, PDL refuses to take any position on them in violation of Local Civil Rule 56.1. In accordance with that rule, Sun served a Statement of Uncontested Facts stating that Sun's concentrated form is not isotonic and that Sun's diluted form is not concentrated. In violation of Rule 56.1, PDL simply refused to take any position on those issues. That is improper. By failing to dispute these key facts, PDL has effectively admitted them under Rule 56.1.

Given the lack of literal infringement, PDL attempts to establish infringement under the doctrine of equivalents. But it ignores a gaping hole in its theory. Sun's concentrated form is [redacted] "isotonic" and, thus, hardly "equivalent." PDL thus argues that Sun's product "becomes" isotonic *after* being diluted by the healthcare provider. But

PDL ignores that dilution brings Sun's product to [redacted] the required concentration limitation, which, again, is hardly "equivalent."

PDL is thus reduced to asserting that Sun's product infringes under the doctrine of "equivalents" because Sun's product and PDL's product are "bioequivalent." But, as many courts have recognized, one thing has nothing to do with the other. The doctrine of equivalents is a legal doctrine comparing the relevant product to the *claims*. Bioequivalence is a regulatory doctrine comparing the relevant product to *another product*, specifically relating to the level of active ingredient in the blood. Under PDL's illogical theory, *all* generic products (which must be bioequivalent for approval) would infringe under the doctrine of equivalents. That is one reason why courts have uniformly rejected such an overly expansive interpretation of the doctrine of equivalents.

In the end, PDL's response brief makes clear that there are no disputed material facts. PDL simply has no basis for continuing to block generic competition. Summary judgment thus should be granted in Sun's favor.

ARGUMENT

As detailed below, Sun's ANDA product does not infringe, either literally or equivalently, with respect to either its concentrated form (because it is not isotonic) or its diluted form (because it is not concentrated).

I. Sun's ANDA Product Does Not Literally Infringe The Asserted Claims.

It is black letter law that a party alleging infringement must prove that the "accused product meets each and every claim limitation." *See, e.g.*, *Forest Labs., Inc. v. Abbott Labs.*, 239 F.3d 1305, 1310 (Fed. Cir. 2001); *accord Builders Concrete, Inc. v. Bremerton Concrete Prods. Co.*, 757 F.2d 255, 257 (Fed. Cir. 1985) (proving "[l]iteral infringement requires that the accused device embody every element of the claim"); *Bayer AG v. Elan Pharm. Research Corp.*, 212

F.3d 1241, 1247 (Fed. Cir. 2000) ("If any claim limitation is absent from the accused device, there is no literal infringement as a matter of law.").

Here, the plain language of the claims require "***a*** pharmaceutical composition" that is ***both*** "isotonic" ***and*** concentrated with "at least about 1 mg/ml nicardipine hydrochloride." (MSJ. Ex. 1 ('405 patent) at col. 10, lines 34-37, 51-60, 64-65; col. 11, lines 5-6, 15-16. (emphasis added).)[1] This is entirely consistent with the patent specification and prosecution history, where PDL made clear that the claimed invention was a single formulation that was both concentrated and directly injectable (meaning it had to be isotonic). (*See, e.g.*, SOF at ¶ 4) (distinguishing prior art by asserting claimed invention is "an *injectable* solution of nicardipine HCl *having a concentration of at least 1 mg/ml*" (emphasis added)); SOF at ¶¶ 20-23 (overcoming PTO rejection by adding concentration limitation of "at least about 1 mg/ml nicardipine hydrochloride," which is an appropriate concentration for direct injection); (SOF at ¶¶ 18, 20-23; SPIL037938-40) (asserting that the "present invention" was to "stabilize" high-concentration solutions, thus distinguishing low concentration solutions in prior art that lacked stability issues).

PDL's infringement arguments ignore the claims' plain language by continually switching their focus back and forth between the concentrated and diluted forms of Sun's product. But PDL offers no principled reason for any such illogical analysis – an analysis that focuses on one form for one claim limitation and a different form for another claim limitation. The Federal Circuit has already rejected a similar argument on similar facts. *See Biogen, Inc. v.*

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[1] References to "MSJ Ex. __" are to the exhibits filed with Sun's July 1, 2008 Motion for Summary Judgment of Noninfringement. References to "SOF" are to Sun's Local Civil Rule 56.1 Statement of Uncontested Facts. References to "Opp. __" are to PDL's Opposition and Cross-Motion for Summary Judgment of Infringement. References to "Ex. __" are to the exhibits submitted with this Reply and Opposition, which are attached to the accompanying Declaration of Melissa Steedle Bogad.

Berlex Labs., Inc., 318 F.3d 1132, 1142 (Fed. Cir. 2003) (finding no infringement of a patent requiring a particular concentration of interferon and rejecting plaintiffs' argument that "a composition that has the claimed concentration of interferon at any time during the production process infringes").

There is no dispute that neither form of Sun's product literally meets both of the disputed limitations at the same time. For the diluted form of Sun's product, each asserted claim requires a concentration of "at least 1 mg/ml" of nicardipine hydrochloride. Sun's diluted product, however, has a concentration of nicardipine hydrochloride that is [redacted] than the claimed concentration. (Sun's MSJ Ex. 5 (12/15/2007 Labeling Amendment) at KRA004555; *accord* SOF at ¶¶ 28-29.)

For the concentrated form of Sun's product, each asserted claim requires an "isotonic" formulation. But Sun's concentrated product is [redacted], not isotonic. In fact, Sun's amended ANDA [redacted] (SOF ¶¶ 34-37); *see Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002) ("summary judgment of no literal infringement [is] properly granted where [an] ANDA specification require[s] the proposed drug to have" characteristics outside the scope of the claims).

Despite that undisputed fact, PDL argues at length that the parties dispute the meaning of "isotonic." (Opp. at 21-26.) But any such alleged dispute is completely irrelevant. Sun's concentrated product – [redacted] – is not "isotonic" under *any* possible definition. The only difference between the parties' proposed interpretations of "isotonic" is that Sun correctly adopts the definition specifically set forth in the '405 patent specification – that is, a fluid with an "osmotic pressure corresponding to that of bodily fluids,"

meaning "approximately 275-300 mOsm/L." (*See* MSJ Ex. 1 ('405 patent) at col. 3, lines 56-64; SOF at ¶¶ 13-15.) But any purported dispute over the meaning of "isotonic" is irrelevant because PDL does not contend that Sun's concentrated product is "isotonic" even under its own definition.

PDL simply cannot deny the dispositive facts that prove Sun does not infringe. So, instead, it avoids them. PDL declined to take any position on the key facts in its Response to Sun's Statement of Uncontested Facts. But "facts submitted in the statement of material facts which remain uncontested by the opposing party are deemed admitted." *Hill v. Algor*, 85 F. Supp. 2d 391, 408 n. 26 (D.N.J. 2000); *accord White v. Camden City Bd. of Educ.*, 251 F. Supp. 2d 1242, 1246 n. 1 (D.N.J. 2003), *aff'd*, 90 Fed. Appx. 437 (3d Cir. 2004); *S.C. v. Deptford Township Bd. of Educ.*, 248 F .Supp. 2d 368, 374 n. 3 (D.N.J. 2003). Thus, by failing to contest the key facts, PDL has effectively admitted them.

Specifically, Sun stated that the "*concentrated form* of Sun's ANDA product is [redacted]" (SOF ¶ 26 (emphasis added).) Instead of providing a responsive answer – as required by Local Civil Rule 56.1 – PDL ignores the statement completely by asserting that Sun's *diluted* product is isotonic. (PDL's Resp. ¶ 26.) But that fails to respond to Sun's statement. With respect to the concentration limitation, Sun stated that the *diluted form* of Sun's product is [redacted] the 'at least about 1 mg/ml nicardipine hydrochloride' concentration required by the claims." (SOF at ¶ 28.) Instead of responding directly, PDL evades the issue by asserting that Sun's *concentrated* product has the required concentration. (PDL's Resp. at ¶ 28.) But, again, that is not responsive.

PDL's refusal to respond directly to these straightforward statements is an admission of both statements under Rule 56.1. And, indeed, there is no possible dispute, as doubly confirmed

by PDL's equivocations. After arguing vigorously that only the *diluted* form is relevant for the "isotonic" limitation (Opp. at 30-34, 37, 40), PDL inconsistently argues that only the *concentrated* form is relevant for the concentration limitation. (*Id.* at 34-35.) But PDL cannot have it both ways. Thus, it remains undisputed that neither the concentrated nor the diluted form of Sun's product constitutes "***a*** pharmaceutical formulation" that meets both disputed limitations.[2]

II. Sun's ANDA Product Does Not Infringe The Asserted Claims Under The Doctrine Of Equivalents.

There is also no material dispute under the doctrine of equivalents. PDL's argument regarding the application of the doctrine of equivalents raises a pure question of law concerning the legal limitations of that doctrine. *See Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 39 n.8 (1997) ("the various legal limitations on the application of the doctrine of equivalents are to be determined by the court," rather than the fact-finder).

A. PDL's Doctrine Of Equivalents Theory Fails As A Matter Of Law For Several Reasons.

For its doctrine of equivalents theory, PDL engages in the same kind of double-talk as it does with respect to literal infringement. PDL starts by expressly abandoning its claim that the diluted form of Sun's product infringes under the doctrine of equivalents. (*See* Opp. at 34-35.) PDL had no choice but to abandon that claim. Sun's diluted form (a) has a concentration of nicardipine hydrochloride that is [redacted], and (b) PDL added the concentration limitation during prosecution and, thus, is precluded by *Festo* from asserting equivalence for that limitation. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535

[2] Contrary to PDL's assertion, the parties do not "agree that there is a material issue of fact for trial" with respect to the terminal sterilization step recited in claim 2. (*See* Opp. at 28 n.10.) Claim 2 requires sterilization by autoclaving while Sun's product is [redacted] In any event, Sun is entitled to summary judgment on claim 2 because, like every other asserted claim, claim 2 requires a formulation that is both isotonic and concentrated.

U.S. 722, 736 (2002) (ruling that "a narrowing amendment made [during prosecution] to satisfy any requirement of the Patent Act may give rise to an estoppel").

But after expressly abandoning its claim of infringement for Sun's diluted form, PDL inconsistently relies exclusively on that form for its equivalence theory. Specifically, it argues that Sun's ANDA product meets the isotonic limitation under the doctrine of equivalents because [redacted] (Opp. at 32; 31; *see also id.* at 30, 33-37.) But PDL is simply describing the diluted formulation, which PDL expressly stated it was *not* accusing of infringement.

Essentially, PDL is relying on a flawed "inducement" theory of infringement. When a party sells a product that does not literally or equivalently infringe – as here, where Sun's concentrated product is [redacted] rather than isotonic – a patentee can establish infringement by "inducement," but only if it can establish that the defendant has "induced" another to engage in "direct infringement." *ACCO Brands, Inc. v. ABA Locks Mfr. Co., Ltd.*, 501 F.3d 1307, 1312 (Fed. Cir. 2007) (citation omitted); *see also* 35 U.S.C. § 271(b).

Here, however, PDL cannot establish direct infringement by *anybody*. True, [redacted] But by doing so, they also [redacted] to well outside the claimed concentration of "at least 1 mg/ml." Thus, no matter which form PDL focuses on, a key element of the claim is completely missing, which means there is no direct infringement and, thus, no infringement by inducement.

The doctrine of equivalents is equally inapplicable when an element is missing. The Supreme Court has explained that "[i]t is important to ensure that the application of the doctrine

[of equivalents], even as to an individual element, is not allowed such broad play as to effectively eliminate that element in its entirety." *Warner-Jenkinson*, 520 U.S. at 29, 40. Thus, "[t]he doctrine of equivalents is not a license to ignore claim limitations." *Dolly, Inc. v. Spalding & Evenflo Cos., Inc.*, 16 F.3d 394, 398 (Fed. Cir. 1994).

Here, any claim of infringement by equivalents for Sun's concentrated formulation would erase the "isotonic" limitation. And any claim of infringement by equivalents for Sun's diluted formulation would erase the "at least 1 mg/ml" limitation. Either way, PDL is attempting to ignore claim limitations in violation of settled law.[3]

PDL could have sought patent protection for a concentrated, [redacted] formulation that, like Sun's product, cannot be directly injected into patients. But it did not do so. Instead, PDL drafted every asserted claim to cover an "*isotonic*" composition "suitable for parenteral administration," which the patent defines as the "administration of a drug by *injecting* a pharmaceutical composition containing such drug." (MSJ Ex. 1 ('405 patent) at col. 1, lines 30-32.)[4] Sun and other members of the public were entitled to rely on the patent's specific language

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[3] *See, e.g., TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.*, 529 F.3d 1364, 1379-80 (Fed. Cir. 2008) (holding that patented telephone that claimed a "dial tone actuating switch electronically connected to said phone line *and* said electronic circuit" was not infringed under the doctrine of equivalents by a competitor's phone in which the actuating switch was connected only to the phone line); *Conopco, Inc. v. May Dep't Stores Co.*, 46 F.3d 1556 (Fed. Cir. 1994) (holding that patented skin care lotion that claimed a combination of two ingredients in a ratio of "about 40:1 to about 1:1" was not infringed by accused product that used a 162.9:1 formulation, and ruling that a finding of infringement under the doctrine of equivalents "would eviscerate the plain meaning of th[e] limitation"); *In re Gabapentin Patent Litig.*, 393 F. Supp. 2d 278, 294 (D.N.J. 2005) (denying doctrine of equivalents theory to claim limitation requiring "less than 20 ppm of an anion of mineral acid" on the grounds that "allowing [the patent owner] to claim a range of equivalents higher than that allowed by the 20 ppm limitation arguably acts to vitiate the claim limitation"); *AK Steel Corp. v. Sollac & Ugine*, 234 F. Supp. 2d 711, 721 (S.D. Ohio 2002) (holding that patent claims requiring up to about 0.5% silicon cannot be infringed under the doctrine of equivalents by an accused process containing 8.0 to 8.5% silicon, because interpreting "0.5% silicon" to encompass 8.0% silicon would vitiate the limitation).

[4] Because the '405 patent further distinguishes between "suitable for parenteral administration" and "administration by infusion," it is clear that the scope of the asserted claims excludes

in assessing the boundaries of the asserted claims. *Freedman Seating Co. v. American Seating Co.*, 420 F.3d 1350, 1362 (Fed. Cir. 2005).

Applying the doctrine of equivalents here would defy not only the plain terms of the claims and the specification (*see* Sun's MSJ at 7-8), but also the patent's prosecution history. During prosecution, PDL asserted that its "invention" was to "stabilize" *concentrated* formulations of nicardipine hydrochloride, which was not an issue for low-concentration formulations that are normally injected immediately upon dilution. (SOF at ¶ 18.) Then, to distinguish its claimed invention from the "crowded" prior art, PDL's main inventor swore to the PTO, "[m]y co-inventors and I set out to make an injectable solution of nicardipine HCl *having a concentration of at least 1 mg/ml*," which is required for direct injection. (SOF at ¶ 4 (emphasis added); *see also* SOF ¶¶ 18, 20-22.) Thereafter, PDL distinguished its "present invention" from prior art nicardipine hydrochloride solutions based on the claimed high concentration. (SOF at ¶ 23; SPIL037938; 037940.)

The stability issue is another fundamental difference between the claimed invention and Sun's diluted product because claim 1 requires a "*stable* pharmaceutical composition." (MSJ Ex. 1 ('405 patent) at col. 10, lines 35-37 (emphasis added).) The whole point of the purported invention was to create a concentrated formulation that could be directly injected and, thus, would need to be sufficiently stable to survive long-term storage measured in *three-month* increments up to a full *three years*. (*Id.* at Table 7; *see also id.* at col. 7, lines 28-31; col. 10, lines 64-65; col. 2, lines 37-41, 60-65; col. 5, lines 5-12; SOF at ¶¶ 4-5); *accord* Opp. at 8

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products that have been diluted with infusion fluids. (*See* MSJ Ex. 1 ('405 patent) at col. 2, lines 37-21: "Thus, there is a need to formulate a stable aqueous pharmaceutical composition of nicardipine hydrochloride, suitable for parenteral administration ***or*** administration by infusion, which may be diluted in additional water or a mixture of water and water-miscible fluids." (emphasis added).)

(emphasizing that claimed invention provides stability up to three years).) As PDL has acknowledged, however, diluted products such as Sun's proposed product are stable only for approximately *24 hours*. (*See* Ex. 1, PDL Published Patent Application No. U.S. 2007/0249689 A1, ¶ 0003 (Oct. 25, 2007).)

After obtaining the '405 patent by strictly limiting the claimed invention to concentrated, stable, injectable isotonic formulations, PDL cannot turn around and rely on the doctrine of equivalents to attempt to recapture what it abandoned during prosecution. A patentee "may not write narrow claims for allowance by the PTO and subsequently attempt to broaden the claims in court by using the doctrine of equivalents." *PSC Computer Prods., Inc. v. Foxconn Int'l, Inc.*, 355 F.3d 1353, 1357 (Fed. Cir. 2004); *Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd.*, 476 F.3d 1321, 1328 (Fed. Cir. 2007) (same).

B. Bioequivalence Does Not Equate To Infringement Under The Doctrine Of Equivalents.

PDL next argues that if Sun's ANDA product is bioequivalent to Cardene® I.V., then it must necessarily infringe the asserted claims of the '405 patent under the doctrine of equivalents. (Opp. at 27, 33-34, 37.) From this faulty premise, PDL concludes that Sun has effectively admitted that its product infringes the '405 patent. (*See* Opp. at 3-4, 14-16, 27, 33-34.)

That is nonsense. Bioequivalence and the doctrine of equivalents are entirely different concepts and, thus, many courts have rejected the notion that infringement is established by bioequivalence. *See, e.g.*, *Abbott Labs. v. Sandoz, Inc.*, 486 F. Supp. 2d 767, 776 (N.D. Ill. 2007) ("[An] admission of bioequivalence is not an admission of infringement under the doctrine of equivalents. They are two distinct concepts.") (citation omitted); *In re Omeprazole Patent Litig.*, 490 F. Supp. 2d 381, 424 (S.D.N.Y. 2007) ("bioequivalence of a product is not an indication that the doctrine of equivalents has been met"); *see also Upjohn Co. v. Mova Pharm. Corp.*, 31 F.

Supp. 2d 211, 215 n. 2 (D.P.R. 1998), *aff'd in relevant part and rev'd in part on other grounds*, 225 F.3d 1306 (Fed. Cir. 2000) (defendant's admission of bioequivalence did not constitute an admission of infringement).

Indeed, equating bioequivalence with infringement would eviscerate the Hatch-Waxman Act, which allows drug manufacturers to market generic versions based on a showing of bioequivalence. 21 U.S.C. § 355(j)(2)(A)(iv). Therefore, if PDL's argument were correct, bioequivalent generic products would *always* infringe, which obviously makes no sense. *See Sandoz, Inc.*, 486 F. Supp. 2d at 776 ("If bioequivalency meant per se infringement, no alternative to a patented medicine could ever be offered to the public during the life of a patent.").

PDL's effort to equate bioequivalence and infringement is particularly illogical in this case. "Bioequivalence" simply means that Sun's product delivers the active ingredient to the circulatory system at essentially the same rate and to essentially the same extent as Cardene® I.V. *See* 21 U.S.C. § 355(j)(8)(B); 21 C.F.R. § 320.1(e); 21 C.F.R. § 320.23(b). It does not mean that Cardene® I.V. and Sun's product have the same *composition* or that they were produced by an equivalent *process*. And, in fact, the two products are very different. Consistent with the claimed invention, Cardene® I.V. is "isotonic" in its concentrated form and, thus, can be directly injected without dilution. PDL admits that Cardene® I.V. is routinely administered by direct injection "off label." (*See* Ex. 2, PDL Published Patent Application No. U.S. 2007/0244166 A1, ¶ 0007 (Oct. 18, 2007).)

Sun's product, by contrast, is [redacted] in its concentrated form and, thus, cannot be directly injected before dilution. Contrary to PDL's argument, Sun is not arguing that "there are safety concerns" associated with the [redacted] (concentrated) version of its product or that its

ANDA product is somehow "less safe" than Cardene® I.V. (*See* Opp. at 3-6; 27.) Sun's product is perfectly safe to administer to patients, but only in the diluted (isotonic) form, as set forth in Sun's product label and contrary to the claims of PDL's patent.

PDL also notes that Sun told the FDA that its product was [redacted] to Cardene® I.V. (Opp. at 4, 14.) But that is just a synonym for "bioequivalent" and obviously does not change the undisputed facts that Sun's concentrated form is [redacted] and Sun's diluted form is not concentrated. (SOF ¶¶ 24-28.)

In the end, Sun's product does not infringe either directly or equivalently because (unlike Cardene® I.V. and unlike the claimed invention) the concentrated product is not isotonic and thus cannot be directly injected. That is a fundamental difference, and far from the kind of "insubstantial" difference contemplated by the doctrine of equivalents.

CONCLUSION

For the reasons set forth above and in Sun's Motion for Summary Judgment of Noninfringement and accompanying Memorandum, this Court should grant Sun's Motion and deny PDL's Cross-Motion for Summary Judgment of Infringement.

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